PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:
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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Applicant's or agent's file reference 700953-53661	Date of mailing (*day/month/year*) 12 JUL 2005 **FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date (*day/month/year*)	Priority date (*day/month/year*)
PCT/US04/37810	12 November 2004 (12.11.2004)	12 November 2003 (12.11.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 48/00; C12N 15/00, 15/63, 15/74, 5/00 and US Cl.: 514/44; 435/320.1, 325, 455

Applicant

THERION BIOLOGICS CORPORATION

1. This opinion contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis(b)* that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Authorized officer Anne Marie S. Wehbe Telephone No. 703-308-1235

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US04/37810

Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material

      ☐ in written format

      ☐ in computer readable form

   c. time of filing/furnishing

      ☐ contained in international application as filed.

      ☐ filed together with the international application in computer readable form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 2 in part, 3, 6-22

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☒ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. 2 in part, 3, 6-22 are so unclear that no meaningful opinion could be formed *(specify)*:

Claim 2 is a multiple dependent claims that depends in the alternative on itself. Claim 2 has only been considered to the extent that it depends on claim 1. Claims 3, and 6-22 are improper multiple dependent claims under PCT Rule 6.4(a).

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 23-24	YES
	Claims 1-2, 4-5	NO
Inventive step (IS)	Claims 24	YES
	Claims 1-2, 4-5, 23	NO
Industrial applicability (IA)	Claims 1-2, 4-5, 23-24	YES
	Claims NONE	NO

2. Citations and explanations:

Claims 1-2, 4, and 5 lack novelty under PCT Article 33(2) as being anticipated by AARTS W. M. et al. Canc. Res. October 15 2002, Vol. 62, 5770-5777. Aarts et al. teaches an avipox vector which encodes CEA and three co-stimulatory molecules, B7-1, ICAM-1 and LFA-3 (Aarts et al., page 5770, abstract and page 5771). Aarts et al. further teaches the generation of anti-CEA immune responses and antitumor activity following administration of the vector (Aarts et al., page 5775-5776). Thus, by teaching all the limitations of the claims as written, Aarts anticipates the instant claims.

Claims 1-2 and 4 lack novelty under PCT Article 33(2) as being anticipated by SCHOLL et al. J. Biomed. Biotech. August 2003, Vol. 3, 194-201. Scholl et al. teaches the generation of antitumor immune responses following the administration of a single vaccinia virus encoding MUC-1 and IL-2 to breast cancer patients (Scholl et al., page 195, and 200). Thus, by teaching all the limitations of the claims as written, Scholl et al. anticipates the instant claims.

Claim 23 lacks an inventive step under PCT Article 33(3) as being obvious over SCHLOM et al. Breast Canc. Res. Treat. 1996, Vol. 38, 27-39 in view of ZAJAC et al. Human Gene Ther. November 1 2003, Vol. 14, 1497-1510. Schlom et al. teaches two different vaccinia viruses encoding the breast cancer antigens MUC-1 and CEA, and the individual use of the vectors to generate anti-tumor responses (Schlom et al., pages 28-29). Zajac et al. supplements Schlom by teaching a single vaccinia vector encoding 3 different tumor antigens (Zajac et al., page 1501, Figure 2). Zajac et al. provides motivation for expressing more than one tumor antigen in the same vector in order to circumvent antigen expression heterogeneity in tumor and immune escape (Zajac et al., page 1498, column 1). Therefore, based on the motivation to express more than one tumor antigen in the same vector, it would have been obvious to modify the vectors taught by Schlom et al. to encode both CEA and MUC-1.

Claim 24 meets the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a single poxvirus vector encoding CEA and a wobbled MUC-1.

Claims 1-2, 4-5, and 23-24 meet the criteria set out in PCT Article 33(4) for industrial applicability as the kits and methods can be used in breast cancer therapy.